Office Action Summary	Application No.	Applicant(s)	
	10/056,348	BURCH ET AL.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38 and 47-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38 and 47-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/14/07 has been entered.

Claim Status

2. Claims 1-37 and 39-46 have been cancelled.

Claims 38, and 47-52 are currently pending.

Claims 38, and 47-52 are being examined in this application.

Priority

3. This application is a continuation of 09/154,354 (filed 9/17/1998; now US Patent 6,552,031), which claims benefit of 60/059,195 (filed 9/17/1997).

4. Applicant's claim for the benefit of a prior-filed applications under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 35 U.S.C. 120, 121, or 365(c) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or

provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, Application No. 09/154,354 and provisional application (US 60//059195), fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

The instant claims are amended to recite "an oral dosage form comprising two analgesic compounds and/or pharmaceutically acceptable salts thereof consisting of (i) nabumetone ... and (ii) oxycodone ...". The instant claims maybe interpreted to recite a method using a composition consisting only two drugs, nabumetone and oxycodone as well as pharmaceutical acceptable salts. However, the claimed priority documents ('354 and '195 application) do not provide support for the instant claimed specific composition.

Thus, the effective filing date for the above said subject matter of the instant application is 1/25/02.

Claim Rejections Maintained

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Baker and others

7. Claims 38, 47-48, 50-52 as amended or originally filed are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 4,569,937 (Baker et al) and Friedel et al (Drugs. 1993. Vol. 45 (1) pages 131-156) and Eversmeyer et al (American Journal of Medicine, Aug. 1993, vol. 95, pages 10S-10S). The previous rejection is maintained for the reasons of record advanced in the previous office actions.

Discussion and Answer to Argument

8. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue "there is no motivation to substitute the ibuprofen in the synergistic combination of the Baker composition with another NSAID," and the combination of the cited references fail to provide motivation to combine. (Reply, pp. 4+).

Contrary to applicant's assertion, the previous office actions (especially, Office action, mailed 10/6/05; pp. 3+; and Office action mailed 8/1/06; pp. 10+) have provided motivation statements to combine the cited references.

Furthermore, applicants are also respectively directed to the recent Supreme Court decision, which forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. *KSR, 127 S.Ct. at 1741, 82 USPQ2d at 1396.* ("Helpful insights, however, need not become rigid and mandatory formulas; and when it is so applied, the TSM test is incompatible with our precedents. The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents.")

Applicants also argue that the Baker reference (and the cited Sunshine reference) does not recite nabumetone. (Reply, pp.6+). Applicants also argue that the structure of "Nabumetone" does not fall within the "five categories" of NSAID recited in the "Sunshine reference". (Reply, pp. 7+).

However, the obviousness rejection as set forth in the previous Office actions is based on the combination of the Baker, Friedel and Eversmeyer references, not a combination of Baker and Sunshine. The Sunshine reference only offers examples of prior art's teaching.

Contrary to applicants' assertion, the Baker reference clearly teaches combining a narcotic analgesic and a NSAID drug (e.g. Col. 1, lines 20+). The Baker reference also clearly teaches the motivation to combine a narcotic analgesic and a NSAID drug. For example, the Baker reference states "the analgesic effect of the combination of a selected NSAID and a

selected narcotic analgesic is greater than for either alone" (col. 1, lines 23-25). This provides ample motivation for a person of ordinary skill in the art to combine a selected NSAID and a selected narcotic analgesic drug to achieve a greater effect.

Furthermore, the Baker reference also teaches the preferred narcotic analgesic is oxycodone, as discussed in the previous Office action, mailed 8/1/06, p. 11, para 3+). The Baker reference does not explicitly teach that nabumetone (a NSAID) is combined with oxycodone. However, Friedel teach nabumetone is a NSAID, and both Friedel and Eversmeyer teach nabumetone offers advantages such as less toxic effect, more safe, and reduced side-effects (Office action, mailed 8/1/06; pp. 12-13). Thus, a person of ordinary skill in the art would have been motivated at the time the invention was made to combine oxycodone and nabumetone as a combination of analgesic compounds to achieve the greater additive effects.

Applicant's argument regarding the structure of nabumetone is irrelevant. Regardless whether nabumetone falls within the "five categories" of NSAID disclosed in Sunshine, the combination of the cited references renders the claimed combination obvious. As discussed previously, the Sunshine reference cited by Baker only provides examples of known NSAID. The term NSAID is known and used in the art to refer to a class of "non-narcotic/non-steroidal anti-inflammatory drugs", which does not exclusively refer to the "five categories of compounds recited in Sunshine. Furthermore, relying on the citation in applicant's reply, the Sunshine reference recites "the compositions and methods of the present invention can be selected from the following categories..." (emphasis added). Clearly, the recitation does not exclude other NSAID.

In addition, as discussed above, other cited references (such as Friedel) teach nabumetone is a known NSAID in the art. Thus, regardless whether Baker or Sunshine recites nabumetone as a NSAID, nabumetone is known as a NSAID in the prior art.

Furthermore, it is not clear which compound the structure provided by applicants in the Reply, p. 8 is representing. First, the chemical structure is not recited anywhere in the instant disclosure. The instant specification does not specifically define the term "nabumetone" with the structure drawn on page 8 of the instant reply. A search in the Merck Index of the said chemical structure reveals the name of the compound to be "Nimesulide" (see The Merck Index Results. "Nimesulide", downloaded from http://themerckindex.cambridgesoft.com/TheMerckIndex/default.asp?; downloaded on 8/10/2007; page 1 only).

The chemical structure for "Nabumetone" as known in the art is also attached (see The Merck Index Results. "Nabumetone", downloaded from http://themerckindex.cambridgesoft.com/TheMerckIndex/default.asp?; downloaded on 8/10/2007; page 2 only), which the structure for nabumetone is different from the structure provided by applicants. The structure for nabumetone as indicated in the Merck Index would fall within the five categories disclosed in Sunshine (see the chemical structures in col.8 of Sunshine).

Applicants also argue "the Eversmeyer and Fiedel reference do not definitively conclude that nabumetone is equally efficacious with less side effects than ibuprofen" and the references teach away from using nabumetone. (Emphasis in original; pp. 9+).

Again, applicants are arguing the specific teaching, suggestion or motivation to combine the cited references. Applicants are also respectively directed to the recent Supreme Court decision, which forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. *KSR, 127 S.Ct. at 1741, 82 USPQ2d at 1396.*

In addition, in arguing the "side effects" of nabumetone as compared to ibuprofen, applicants seem to argue that nabumetone would not be enabled for various treatments (such as treatment for pain) because of the negative side effects.

Contrary to applicant's assertion, the Friedel and Eversmeyer references do not teach away from using nabumetone. As stated by the applicants, "these references are inconclusive at best" and does not teach that nabumetone cannot be used as a drug for treatment. Because the cited references do teach the potential benefit of nabumetone such as less toxic effect, more safe, and reduced side-effects (Office action, mailed 8/1/06; pp. 12-13), one of ordinary skill in the art would have been motivated at the time the invention was made to combine oxycodone and nabumetone for the synergistic effects of the said drugs.

Applicants also argue "the Examiner is not considering the invention as a whole" and only focusing on "nabumetone". (Reply, pp. 11+).

Contrary to applicants' assertion, the rejections over the instant claims are based on a combination of references that teach every element of the claimed invention, and not just nabumetone. As discussed in the previous office actions as well as the discussions above, the instant claimed invention is considered as a whole. That is a method of treatment using a

combination of nabumetone and oxycodone is rendered obvious by the cited combination of references.

Applicants also argue that the examiner has not considered the side effects of "oxycodone", and listing numerous side effects of the drug. (Reply, pp. 11).

Again, in listing the "side effects" of oxycodone, applicants seem to argue that oxycodone would not be enabled for various treatments (such as treatment for pain) because of the negative side effects. Thus, the combination of nabumetone and oxycodone would not be enabled for various therapeutic treatments.

Although, both nabumetone and oxycodone both have individual side effects, both of the said drugs have been successfully used for various treatments, as evidenced by the cited references.

Applicants also argue "the Examiner is relying on an improper 'obvious to try' rationale" (Reply, p.12).

Again, applicants are respectively directed to the previous rejections for motivation statements to combine.

In addition, "When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103." (emphasis added; *KSR, 127 S.Ct. at 1741, 82 USPQ2d at 1396).*

Applicants also argue "the Examiner is improperly picking and choosing ibuprofen and oxycodone from the prior art". (Reply, pp. 12+).

Applicants supported the above assertion by arguing over the Baker reference alone. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants argue "the Examiner is improperly relying on In re Kerkhoven" because the said case law is with respect to "combining references", and the rejections are based on "modifying" the Baker reference. (Reply, p.18).

However, the purported "modifying" is based on the "combination of references".

Baker and others con't

9. Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Baker et al. '937 and Friedel et al. Drugs Vol. 45(1): pages 131-156 1993) and/or Eversmeyer et al. as applied to claims 38, 47-48 and 50-52 above, and further in view of Oshlack et al. US Pat. No. 5,472,712 (12/95) or Oshlack et al. US Pat. No. 6,294,195 (9/01: effectively filed 10/93 or earlier). The previous rejection is maintained for the reasons of record as set forth in the previous office actions.

Discussion and Answer to Argument (103 art rejection)

10. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants traversed the above rejection with the same argument as the traversal over the combinations of "Baker and others" references. Thus, applicants are respectively directed to the discussion under the "Baker and others" for answer to arguments.

New Claim Rejections

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter Rejection

12. Claims 38 and 47-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 38 has been amended to recite "an oral dosage form comprising two analgesic compounds and/or pharmaceutically acceptable salts thereof consisting of (i) nabumetone ... and (ii) oxycodone ...". The instant claims maybe interpreted variously, such as a method using a

composition consisting only two drugs, or a method using a composition comprising pharmaceutical acceptable salts and the said salts consist of "nabumetone" and "oxycodone", etc. However, the instant specification does not provide adequate support for the recited composition as one of skilled in the art can reasonable broadly interpret the instant claims.

If Applicant believes this rejection is in error, applicant must disclose where in the specification support for the entire scope of the amendment(s) and/or new claims can be found. As a result, Claims 38 and 47-52 represent new matter.

Second paragraph of 35 U.S.C. 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 38 and 47-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 38 has been amended to recite "an oral dosage form comprising two analgesic compounds and/or pharmaceutically acceptable salts thereof consisting of (i) nabumetone ... and (ii) oxycodone ...". The instant claims maybe interpreted variously, such as a method using a composition consisting only two drugs, or a method using a composition comprising pharmaceutical acceptable salts and the said salts consist of "nabumetone" and "oxycodone",.etc. It is not clear for which phrase the transition phrase "consisting of " is modifying. The transition phrase "consisting of" maybe interpreted to modify the "oral dosage form", which interpretation

would be in conflict with the transition phrase, "comprising". If the term "consisting of" is modifying other terms such as "two analgesic compounds" or "pharmaceutically acceptable salts", then the different interpretation would lead to different compositions used by the claimed method. Thus, one of ordinary skill in the art would not be able to apprise the metes and bounds of the claimed invention.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(Note: the instant claim numbers are in bold font.)

16. Claims 38, 47-50 and 52 are rejected under **35 U.S.C. 102(b)** as being anticipated by Mayer et al (US 5,840,731; 11/24/1998; filed on 8/2/1995). As discussed above, the priority benefit of the instant application to earlier filed applications is denied, and thus the effective filing date of the instant application is 1/25/02).

Mayer et al, throughout the patent, teach methods of treating pain using various drug compositions (see Abstract; Claim 2), which reads on the claimed treatment method of **clm 38**.

The reference also teaches the compositions of drugs can be combinations of drugs (e.g. col.1, lines 24+), and especially combination between Opioid analgesics and NSAIDS (e.g. col.1, lines 50+). The reference also teaches "the first component of the drug composition" is a opioid

such as "oxycodone" (e.g. col.3, liens 57+). The reference also teaches "the second component of the drug composition" is "of the nonopioid type... of any of the foregoing" (col.4, lines 11+), and the reference discloses the nonopioid analgesics includes "nabumetone" (col.3-4; bridging). These passages of the reference teach a composition for pain treatment comprising oxycodone and nabumetone of **clm 38**.

The reference also teaches pharmaceutical acceptable carriers (col. 5), which reads on the component of **clms 38, 48**. The reference also teaches, for example, 4.5 mg of oxycodone (see Table in between cols. 5-6), which reads on the dosage amount of **clm 52**.

The reference also teaches various amounts of the "first" and "second" components of the drug (e.g. col.5-6; Examples), which read on the ration recited in **clm 47**.

The reference also teaches using various drug formulations such as gelatin capsules (e.g. col5, lines 5+), which reads on the sustained release carriers of **clms 49 and 50**.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1639
8/10/07

/Jon D. Epperson/
Primary Examiner, AU 1639